

# OFF=LABEL USE OF DONEPEZIL FOR CHRONIC CONFABULATION IN A 50-YEAR OLD PATIENT WITH TRAUMATIC BRAIN INJURY

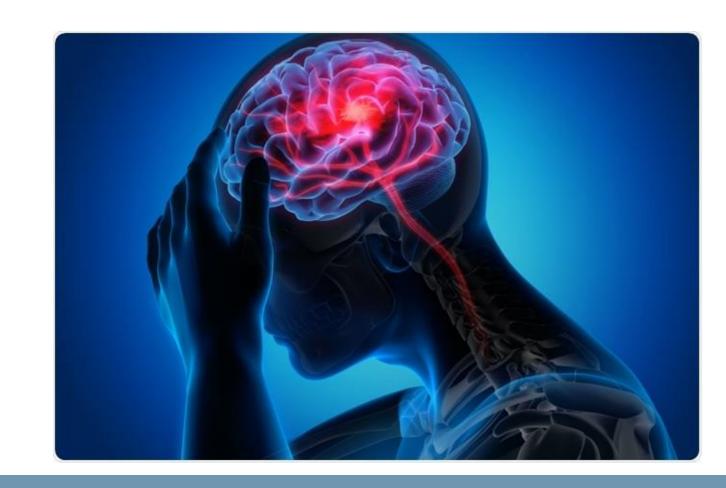


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#### BACKGROUND

- Confabulation is a memory impairment in which gaps in a person's memory are filled with fabricated or distorted information.
- In traumatic brain injury (TBI), confabulation may occur due to damage to acetylcholinerich structures, such as the hippocampus, and cortical cholinergic pathways that are involved in various cognitive domains including memory and attention.
- No treatment has been approved for confabulations or memory disturbances in the TBI population, though research has shown positive effects on memory in adult Alzheimer's Disease patients with the use of central acetylcholine modulators, such as donepezil.
- Donepezil has thus been used off-label, with limited evidence, to help further neuro-recovery after TBI.



#### MATERIALS AND METHODS

Health Insurance Portability and Accountability
 Act (HIPAA) authorization was obtained for
 this case report. The report is devoid of
 patient identifiable information, it is exempt
 from IRB review requirements per University
 of Rochester policy

#### RESULTS/CASE REPORT

#### Case description: presentation to acute rehabilitation admission

A 50-year old male presented with functional and cognitive decline after a fall from a ladder at work. His presenting Glasgow Coma Scale (GCS) score was 9. Imaging showed left temporal subdural and epidural hemorrhages, subarachnoid hemorrhage, as well as multifocal intraparenchymal hemorrhages most notable in the right fronto-parietal lobes. During his hospital course, he was started on amantadine, which was continued on admission to the acute rehabilitation unit, where his cognitive function per Ranchos Los Amigos Scale (RLAS) was IV.

#### Case description: acute rehabilitation admission to discharge

In acute rehabilitation, neuropsychology evaluation showed inattentiveness, and physical, occupational, and speech therapy providers noted disorientation to time and place, dysarthric speech, and impairment in attention and memory. Though the patient's cognitive function steadily improved to RLAS VII by day 28 of acute rehabilitation, he began to develop visual hallucinations and was subsequently weaned off amantadine.

One month after admission, the patient developed a persistent confabulatory state which began to hinder his progress in therapy. Methylphenidate was then started to help with attention and arousal during the day, but this had little effect on his persistent delirium and frequent tangential confabulations. For his refractory confabulation, a trial of 5 mg donepezil was initiated, which was then increased to 10 mg one month later.

Per daily rehabilitation team assessments, his cooperation with medical care significantly improved and he had all but stopped making confabulatory statements within 2 weeks of starting donepezil. The patient went on to spend 140 days in acute rehabilitation and showed improved participation in daily physical, occupational, and speech therapy after starting donepezil.

Unfortunately, his rehab course was complicated by a pulmonary embolism (PE) and he was transferred to the intensive care unit for further medical management. He was continued on donepezil for the remainder of his hospital stay and after discharge to a short-term nursing facility (SNF).

#### Case diagnosis

Confabulation secondary to TBI.

#### Follow-up results

Upon follow-up 3 months later, he was released to go home with home health services and intermittent supervision. No confabulations were observed or reported during the visit.

Key Functional Changes/Improvements	
Admission	RLAS IV, on amantadine
Day 7	Visual hallucinations, amantadine weaned over 2 weeks
Day 8, 22, 28	RLAS V, VI, VII, respectively
Day 50	Methylphenidate started for attention/arousal, no effect on confabulation
Day 85	Donepezil 5mg initiated
Day 109	Recreational therapist first documents improvement in confabulations; PT and OT notes indicate increased participation
Day 120	Donepezil increased to 10mg
Day 133	Therapists begin to note resurgence of confabulations
Day 141	Patient transferred to ICU for PE
Day 240	Patient discharged from acute hospital to SNF
3-month follow-up	Discharge from SNF to home approved by PM&R Brain Injury attending; chronic confabulatory state resolved

## Figure 1: timeline detailing patient hospital and rehabilitation course.

RLAS = Rancho Los Amigos Scale

SNF = Short-term Nursing Facility

PT/OT = Physical Therapy/Occupational Therapy

#### DISCUSSION AND CONCLUSION

- Cognitive impairment due to TBI can be more debilitating than resulting physical disabilities. One proposed mechanism of cognitive dysfunction after TBI is damage to acetylcholine-rich structures and pathways.
- Donepezil, a reversible acetylcholine modulator that has high specificity for brain tissue, is used off-label to help further neurorecovery after TBI.
- In this case, a positive outcome with resolution of confabulation was obtained after a total 8 months of donepezil therapy and intensive rehabilitation. Initial improvements in confabulations were observed as early as two weeks after starting donepezil.
- If patients are not improving with medications targeting dopamine or norepinephrine, as in our patient's case, consideration of medications that target acetylcholine, such as donepezil, may yield meaningful cognitive improvements.
- Further research needs to be conducted to determine ideal patient populations and treatment protocols for donepezil use in TBI.

#### REFERENCES

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